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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: **MODIFIED BYRODIN 1 WITH REDUCED IMMUNOGENICITY**

(57) Abstract: The invention relates to the modification of bryodin 1 to result in bryodin 1 proteins that are substantially non-immunogenic or less immunogenic than any non-modified counterpart when used in vivo. The invention relates furthermore to T-cell epitope peptides derived from said nonmodified protein by means of which it is possible to create modified bryodin 1 variants with reduced immunogenicity.



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## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 03/06055

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61K47/48

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBL, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 34317 A (ADAIR FIONA SUZANNE ;CARR FRANCIS JOSEPH (GB); HAMILTON ANITA ANNE) 15 June 2000 (2000-06-15) cited in the application the whole document See especially Example 4 and Figure 10 ---	1-16
A	WO 98 52976 A (BIOVATION LTD ;CARR FRANCIS J (GB)) 26 November 1998 (1998-11-26) ---	
A	ALTUVIA Y ET AL: "RANKING POTENTIAL BINDING PEPTIDES TO MHC MOLECULES BY A COMPUTATIONAL THREADING APPROACH" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 249, no. 1, 1995, pages 244-250, XP000925520 ISSN: 0022-2836 --- -/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
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- \*O\* document referring to an oral disclosure, use, exhibition or other means
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- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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- \*Z\* document member of the same patent family

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/06055

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>SPENCER D I R ET AL: "A STRATEGY FOR MAPPING AND NEUTRALIZING CONFORMATIONAL IMMUNOGENIC SITES ON PROTEIN THERAPEUTICS" PROTEOMICS, XX, XX, vol. 2, no. 3, March 2002 (2002-03), pages 271-279, XP009009265</p>	
A	<p>MEISTER G E ET AL: "Two novel T cell epitope prediction algorithms based on MHC-binding motifs; comparison of predicted and published epitopes from Mycobacterium tuberculosis and HIV protein sequences" VACCINE, BUTTERWORTH SCIENTIFIC, GUILDFORD, GB, vol. 13, no. 6, 1 April 1995 (1995-04-01), pages 581-591, XP004057605 ISSN: 0264-410X</p>	
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A	<p>MOOLA Z B ET AL: "ERWINIA CHRYSANTHEMI L-ASPARAGINASE: EPI TOPE MAPPING AND PRODUCTION OF ANTIGENICALLY MODIFIED ENZYMES" BIOCHEMICAL JOURNAL, PORTLAND PRESS, LONDON, GB, vol. 302, no. PART 3, 1994, pages 921-927, XP000918634 ISSN: 0264-6021</p>	
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A	<p>SALI A ET AL: "COMPARATIVE PROTEIN MODELLING BY SATISFACTION OF SPATIAL RESTRAINTS" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 234, 1993, pages 779-815, XP002948615 ISSN: 0022-2836</p>	
	<p style="text-align: center;">-/--</p>	

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/06055

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>KWOK W W ET AL: "Rapid epitope identification from complex class-II-restricted T-cell antigens" TRENDS IN IMMUNOLOGY, ELSEVIER, CAMBRIDGE, GB, vol. 22, no. 11, 1 November 2001 (2001-11-01), pages 583-588, XP004319746 ISSN: 1471-4906</p> <p>----</p>	
T	<p>WO 02 069232 A (MERCK PATENT GMBH ; CARTER GRAHAM (GB); JONES TIM (GB); CARR FRANCI) 6 September 2002 (2002-09-06)</p> <p>----</p>	
A	<p>GAWLAK SUSAN L ET AL: "Molecular, biological, and preliminary structural analysis of recombinant bryodin 1, a ribosome-inactivating protein from the plant Bryonia dioica." BIOCHEMISTRY, vol. 36, no. 11, 1997, pages 3095-3103, XP002256641 ISSN: 0006-2960 cited in the application -&amp; DATABASE EMBL 'Online! 21 November 2001 (2001-11-21) GAWLAK, S L. ET AL.: "Ribosome-inactivating protein 'Bryonia dioica!" retrieved from EMBL Database accession no. AAL34334 XP002256642 the whole document</p> <p>----</p>	
A	<p>US 5 541 110 A (SIEGALL CLAY B) 30 July 1996 (1996-07-30) cited in the application</p> <p>----</p>	
A	<p>STIRPE F ET AL: "BRYODIN A RIBOSOME-INACTIVATING PROTEIN FROM THE ROOTS OF BRYONIA-DIOICA L. WHITE BRYONY" BIOCHEMICAL JOURNAL, vol. 240, no. 3, 1986, pages 659-666, XP009018531 ISSN: 0264-6021</p> <p>----</p>	
A	<p>BATTELLI M G ET AL: "TOXICITY OF AND HISTOLOGICAL LESIONS CAUSED BY RIBOSOME-INACTIVATING PROTEINS THEIR IGG-CONJUGATES AND THEIR HOMOPOLYMERS" APMIS, vol. 98, no. 7, 1990, pages 585-593, XP009018529 ISSN: 0903-4641</p> <p>----</p>	
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## INTERNATIONAL SEARCH REPORT

International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>FRYXELL DANIEL K ET AL: "Identification of a specific tyrosine residue in Bryodin 1 distinct from the active site but required for full catalytic and cytotoxic activity"</p> <p>PROTEIN SCIENCE, vol. 7, no. 2, February 1998 (1998-02), pages 318-324, XP009018559 ISSN: 0961-8368</p> <p>-----</p>	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claim : 14 and 15

A peptide part of Bryodin 1 comprising one or more T-cell epitopes.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 03/06055

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/06055

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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